AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1 (Original): A method of administering a bioactive agent to cells of a targeted tissue site of a subject which comprises administering to said subject an effective amount of the bioactive agent as a bioconjugate, wherein said bioconjugate comprises the bioactive agent and an organocobalt complex wherein the bioactive agent is covalently conjugated to the cobalt atom through a non-reactive atom in the bioactive agent molecule, and wherein said bioconjugate is actively transported into said cells of said targeted tissue site and accumulates in an inactive form until activated by cleavage of the bioactive agent from the organocobalt complex.

2 (Original): The method of claim 1, wherein the cleavage occurs as the result of cellular displacement.

3 (Original): The method of claim 1, wherein the cleavage occurs as the result of cellular B_{12} metabolic enzymes.

4 (Original): The method of claim 1, wherein the cleavage is caused by an external signal.

5 (Original): The method of claim 4, wherein said external signal is applied to the targeted tissue site.

6 (Original): The method of claim 4, wherein said external signal is visible light of a wavelength which causes photolysis of said bioconjugate.

7 (Original): The method of claim 6, wherein said visible light has a wavelength of 400-800 nm.

8 (Original): The method of claim 6, wherein said visible light has a wavelength of 600-800 nm.

9 (Original): The method of claim 6, wherein said visible light has a wavelength of 600-750 nm.

10 (Original): The method of claim 6, wherein said visible light is delivered by fiber optics.

11 (Original): The method of claim 6, wherein the area surrounding said targeted tissue site is subjected to a magnetic field which serves to encourage recombination of photolyzed bioconjugate outside the targeted tissue site and thereby reduce the amount of bioactive agent available to healthy tissues.

12 (Original): The method of claim 4, wherein said external signal is ultrasound of a frequency which causes sonolysis of said bioconjugate.

13 (Original): The method of claim 12, wherein said ultrasound has a frequency in the range of between about 20 kHz to 500 MHz.

14 (Original): The method of claim 12, wherein said ultrasound has a frequency in the range of between about 20 kHz to 100 MHz.

15 (Original): The method of claim 12, wherein said ultrasound has a frequency in the range of between about 20 kHz to 10 MHz.

16 (Original): The method of claim 1, wherein said targeted tissue site is neoplastic tissue and said bioactive agent is an anticancer agent.

17 (Original): The method of claim 16, wherein said neoplastic tissue is tissue of a sarcoma.

18 (Original): The method of claim 16, wherein said neoplastic tissue is tissue of a carcinoma.

19 (Original): The method of claim 16, wherein said neoplastic tissue is tissue of a leukemia.

20 (Original): The method of claim 1, wherein said targeted tissue site is tissue afflicted with psoriasis and said bioactive agent is a cytotoxic agent or anti-metabolite.

21 (Original): The method of claim 1, wherein said targeted tissue site is tissue for the application of gene therapy and said bioactive agent is an oligonucleotide or a polynucleotide.

22 (Original): The method of claim 21, wherein said oligonucleotide is antisense DNA or RNA.

23 (Original): The method of claim 1, wherein said targeted tissue site is tissue for the application of peptide therapy and said bioactive agent is a peptide or protein.

24 (Original): The method of claim 1, wherein a bolus of vitamin B_{12} is administered prior to administration of said bioconjugate.

25 (Original): The method of claim 1, wherein vitamin B_{12} is administered intravenously after cleavage of the bioconjugate to wash out uncleaved bioconjugate.

26 (Original): The method of claim 1, wherein nitrous oxide is administered first to deplete body stores of vitamin B_{12}.

27 (Original): The method of claim 1, wherein said non-reactive atom is selected from the group consisting of a carbon atom, a nitrogen atom, an oxygen atom, a sulfur atom, a selenium atom or a silicon atom.

28 (Original): The method of claim 1, wherein said non-reactive atom is a carbon atom.

29 (Original): The method of claim 1, wherein the non-reactive carbon atom is a carbon atom from an alkyl, acyl or aryl group that will not lead to rearrangement or destruction of the bioactive agent under conditions of ligand exchange during receptor-mediated endocytosis.

30 (Original): The method of claim 1, wherein said bioactive agent is covalently bound directly to the cobalt atom of the organocobalt complex.

31 (Original): The method of claim 1, wherein said bioactive agent is covalently bound indirectly to the cobalt atom of the organocobalt complex via a spacer.

32 (Currently amended): The method of claim 31, wherein said spacer is a self-destructing linker.

33 (Original): The method of claim 1, wherein said bioactive agent is a diagnostic compound.

34 (Original): The method of claim 1, wherein said bioactive agent is a drug.

35 (Original): The method of claim 1, wherein said bioactive agent is an anticancer agent.

36 (Original): The method of claim 1, wherein said bioactive agent is a peptide, peptide analogue, protein or protein analogue.

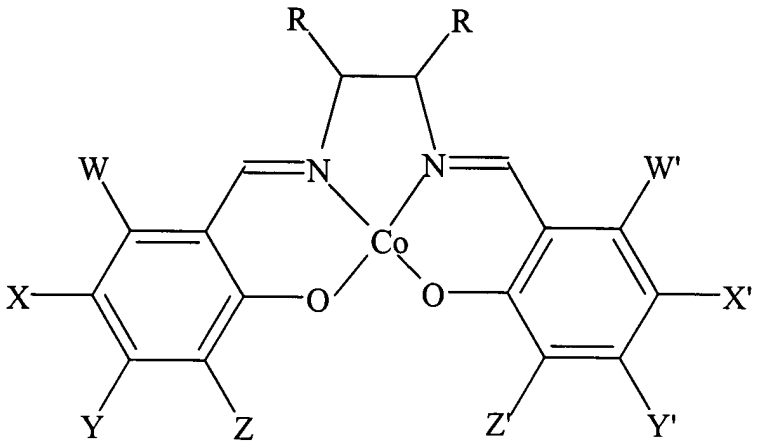
37 (Original): The method of claim 1, wherein said bioactive agent is a nucleic acid or a nucleic acid analogue.

38 (Original): The method of claim 37, wherein said nucleic acid or nucleic acid analogue is a polynucleotide, oligonucleotide, antisense DNA or antisense RNA.

39 (Currently amended): The method of claim 1, wherein said organocobalt complex is cobalamin, cobalamin lactone, cobalamin lactam, or a cobalamin derivative ~~or a cobalamine analogue~~, wherein said cobalamin derivative is (a) cobalamin in which the benzimidizaole ring is substituted with a halogen, hydroxy or a C_{1-6} alkyl, (b) an anilide, ethylamide, monocarboxylic acid,

dicarboxylic acid, tricarboxylic acid or proprionamide derivative of cobalamin, or (c) cobalamin substituted with an amino, a nitro, a halogen, a sulfito, a C_{2-6} alkylene or a C_{2-6} alkyne.

40 (Currently amended): The method of claim 1, wherein said organocobalt complex is a compound having the following formula:



wherein ~~the substituents may be included or omitted to modulate physical properties of the molecule, e.g., water solubility, stability of λ_{max} -- the wavelength at which the complex absorbs~~ R is H, amino, C_{1-6} alcohol, or C_{1-6} carboxyl, W, W', X, X', Y, Y', Z and Z' are independently H, amino, C_{1-6} alcohol, C_{1-6} carboxyl, SO_3-, CH_2OH, CO_2H, or nitro, or W and X together form a 4-6 member cyclic or heterocyclic ring, or W' and X' together form a 4-6 member cyclic or heterocyclic ring, or Y and Z together form a 4-6 member cyclic or heterocyclic aromatic ring or Y' and Z' together form a 4-6 member cyclic or heterocyclic aromatic ring.

41 (Currently amended): The method of claim 40 which further comprises a targeting molecule covalently linked to one of said R, W, W', X, X', Y, Y', Z or Z, wherein said targeting molecule is selected from the group consisting of glucose, galactose, mannose, mannose 6-

phosphate, transferrin, cobalamin, asialoglycoprotein, α-2-macroglobulins, insulin, a peptide growth factor, folic acid or derivatives, biotin or derivatives, $YEE(GalNAcAH)_3$ or derivatives, albumin, texaphyrin, metallotexaphyrin, a vitamin, a coenzyme, an antibody, an antibody fragment and a single-chain antibody variable region (scFv).

42 (Currently amended): The method of claim 1, wherein said organocobalt complex is selected from the group consisting of organo(pyridine)bis(dimethylglyoximato)cobalt, a corrinoid, or derivatives thereof ~~and analogues thereof~~, wherein said derivative is (a) a corrinoid in which the benzimidizaole ring is substituted with a halogen, hydroxy or a C_{1-6} alkyl, (b) a corrinoid substituted with an amino, a nitro, a halogen, a sulfito, a C_{2-6} alkylene or a C_{2-6} alkyne, or (c) organo(pyridine)bis(dimethyl-glyoximato)cobalt substituted with an amino, a nitro, a halogen, a sulfito, a C_{2-6} alkylene or a C_{2-6} alkyne.

43 (Original): The method of claim 1, wherein said organocobalt complex comprises a multiple unsaturated heterocyclic ring system bonded to a cobalt atom through 4-5 nitrogens and/or chalcogens which are part of said ring system.